#11/13

NOV 2 0 2002 W

```
A TRADE MA
<110> Manoharan,
      Guzaev, Andrei P.
<120> Labeled Oligonucleotides, Methods For Making Same, And Compounds Useful Therefor
<130>
       ISIS-4723
<140>
       09/823,031
      2001-03-30
<141>
                                                                      RECEIVED
<160>
                                                                        NOV 2 5 2002
<170>
       PatentIn version 3.1
<210>
                                                                   TECH CENTER 1600/2900
<211>
       12
<212>
       DNA
<213>
      Artificial Sequence
<220>
<223>
      Synthetic Oligonucleotide Sequence
<400> 1
ttttttttt tt
                                                                       12
<210>
<211>
       20
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223>
       Synthetic Oligonucleotide Sequence
<400> 2
atgcattctg cccccaagga
                                                                       20
<210>
<211>
       20
<212>
<213>
       Artificial Sequence
<220>
<223>
       Synthetic Oligonucleotide Sequence
<220>
      misc_feature
<221>
<222>
       (1)...(6)
<223> 2'-O-(2-methoxyethyl)
<220>
<221>
      misc_feature
<222>
       (15)..(20)
<223> 2'-O-(2-methoxyethyl)
<220>
<221>
       misc_feature
<222>
       (3)..(3)
<223>
       5-methyl-2'-O-(2-methoxyethyl) cytidine
<400> 3
agcttctttg cacatgtaaa
                                                                       20
```

<210> 4

```
20
<211>
<212>
       Artificial Sequence
<213>
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221>
       misc_feature
<222>
       (1)..(1)
       dimethoxytrityl protecting group
<223>
<220>
<221>
      misc_feature
<222>
       (20)...(20)
<223>
       3' phosphate group
<400> 4
tgcatcccc aggccaccat
                                                                         20
<210>
<211>
       20
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223>
       Synthetic Oligonucleotide Sequence
<220>
<221>
       misc_feature
<222>
       (1)..(1)
<223>
       dimethoxytrityl protecting group
<220>
<221> misc_feature
<222> (20)..(20)
<223>
      3' phosphorothioate group
<400> 5
tgcatcccc aggccaccat
                                                                         20
<210>
<211>
       20
<212>
       DNA
<213> Artificial Sequence
<220>
<223>
       Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222>
       (20) . (20)
<223>
      3' phosphate group
<400> 6
tgcatccccc aggccaccat
                                                                         20
<210>
<211>
       20
<212>
      DNA
<213>
     Artificial Sequence
<220>
```

```
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222>
       (20)^{-}. (20)
<223> 3' phosphorothioate group
<400> 7
tgcatccccc aggccaccat
                                                                       20
<210>
       8
       20
<211>
<212>
      DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222>
       (20) ... (20)
<223> N-(1-pyrenylmethyl) iodoacetamide linked to a 3' phosphorothioate
<400> 8
tgcatcccc aggccaccat
                                                                       20
<210>
       9
<211>
       20
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222>
      (20)..(20)
<223> 5-iodoacetamidofluorescein linked to a 3' phosphorothioate group
<400> 9
tgcatcccc aggccaccat
                                                                       20
<210>
      10
<211>
       20
<212>
      DNA
<213> Artificial Sequence
<220>
<223>
      Synthetic Oligonucleotide Sequence
<220>
<221>
      misc_feature
<222>
      (2)..(2)
<223> modified phosphorothioate group
<220>
<221> misc_feature
<222>
      (20)...(20)
<223> modified phosphorothicate group
<400> 10
tgcatcccc aggccaccat
                                                                       20
```

```
<210> 11
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
       Synthetic Oligonucleotide Sequence
<223>
<220>
<221> misc_feature
<222>
       (1)...(1)
<223> modified phosphorothioate groups
<220>
<221> misc_feature
<222>
       (20)..(20)
<223> modified phosphorothioate groups
<400> 11
tgcatcccc aggccaccat
                                                                            20
<210> 12
<211>
       20
<212> DNA
<213> Artificial Sequence
<220>
<223>
      Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222>
       (1)..(1)
<223> cholesterol and linker or dialkylglycerol and linker
<400> 12
gcccaagctg gcatccgtca
                                                                            20
<210> 13
<211>
       20
<212>
       DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222> (1)..(1)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222>
      (1)..(1)
<223> cholesterol and linker
<220>
<221> misc_feature
<222> (15)..(15)
<223> t: 2'-O-MOE-rT
```

<220>

```
<221> misc_feature
<222> (2)..(3)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (16)..(16)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (17)..(17)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature <222> (18)..(20)
<222> (18)..(20)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (13)..(14)
<223> c: 2'-O-MOE-5-Me-rC
<400> 13
tccgtcatcg ctcctcaggg
                                                                                                 20
<210> 14
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222> (1)..(1)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222>
         (1)..(1)
<223> cholesterol and linker
<220>
<221> misc_feature
<222> (16)..(16)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (17)..(17)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (18)..(20)
<223> g: 2'-O-MOE-rG
```

Market A

```
<220>
<221> misc_feature
<222> (2)..(2)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (3)..(4)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (5)..(5)
<223> a: 2'-O-MOE-rA
<400> 14
gtccaccatt agcacgcggg
                                                                                              20
<210> 15
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222> (1)..(1)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222>
         (1)...(1)
<223> cholesterol and linker
<220>
<221> misc_feature
<222> (2)..(2)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (3). (4)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (5)..(5)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature
<222> (6)..(7)
<223> C*: 5-Me-dC
<220>
<221> misc_feature
<222> (13)..(13)
<223> C*: 5-Me-dC
```

Page 6

```
<220>
<221> misc_feature
<222> (15)..(15)
<223> C*: 5-Me-dC
<220>
<221> misc_feature
<222> (16)..(16)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (17)..(17)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (18)..(20)
<223> g: 2'-O-MOE-rG
<400> 15
gtccaccatt agcacgcggg
                                                                                              20
<210> 16
<211> 18
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222> (1)..(2)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222>
         (1)..(1)
<223> cholesterol and linker
<220>
<221> misc_feature
<222> (3)..(3)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (4)..(4)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (5)..(6)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (7)..(7)
<223> a: 2'-O-MOE-rA
```

Page 7

```
<220>
<221> misc_feature
<222> (8)..(9)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (10)..(10)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (11)..(11)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (12)..(12)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature
<222> (13)...(13)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (14)..(15)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (16)..(16)
<223> 2'-O-MOE-rA
<220>
<221> misc_feature
<222> (17)..(17)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (18)..(18)
<223> a: 2'-O-MOE-rA
<400> 16
cctcttacct cagttaca
                                                                                                18
<210> 17
<211> 18
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature <222> (1)..(1)
```

Page 8

```
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (1)..(1)
<223> cholesterol and linker
<220>
<221> misc_feature
<222> (10)..(11)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (12)..(13)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature
<222> (14)..(16)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (17)..(17)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature
<222> (18)..(18)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (2). (2)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (3)..(3)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (4)..(4)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature
<222> (5)..(6)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (7)..(7)
<223> a: 2'-O-MOE-rA
<220>
<221> misc_feature
```

```
<222> (8)..(9) * 
<223> c: 2'-O-MOE-5-Me-rC
   <400> 17
   gctattacct taacccag
   <210> 18
   <211>
           20
   <212> DNA
   <213> Artificial Sequence
   <220>
   <223> Synthetic Oligonucleotide Sequence
   <220>
   <221> misc_feature
  <222> (1)..(1)
<223> c: 2'-O-MOE-5-Me-rC
   <220>
  <221> misc_feature
<222> (1)..(1)
   <223> cholesterol and linker
  <220>
  <221> misc_feature
<222> (2)..(2)
<223> t: 2'-O-MOE-rT
  <220>
  <221> misc_feature
<222> (3)..(3)
<223> g: 2'-O-MOE-rG
  <220>
  <221> misc_feature
  <222> (4)..(4)
<223> c: 2'-O-MOE-5-Me-rC
  <220>
   <221> misc_feature
  <222> (5)..(5)
<223> t: 2'-O-MOE-rT
<220>
  <221> misc_feature
  <222> (8)..(9)
   <223> C*: 5-Me-dC
  <220>
  <221> misc_feature
<222> (11)..(11)
<223> C*: 5-Me-dC
  <220>
  <221> misc_feature
<222> (16)..(18)
<223> t: 2'-O-MOE-rT
```

<220>

Page 10

18

```
<221> misc feature
<222> (19)..(19)
<223> g: 2'-O-MOE-rG
<220>
<221> misc_feature
<222> (20)..(20)
<223> a: 2'-O-MOE-rA
<400> 18
ctgctagcct ctggatttga
<210> 19
<211>
         20
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic Oligonucleotide Sequence
<220>
<221> misc_feature
<222> (1)..(1)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222>
        (1)...(1)
<223> cholesterol and linker
<220>
<221> misc_feature
<222> (4)..(4)
<223> c: 2'-O-MOE-5-Me-rC
<220>
<221> misc_feature
<222> (5)..(5)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (8)..(8)
<223> C*: 5-Me-dC
<220>
<221> misc_feature
<222> (11)..(12)
<223> C*: 5-Me-dC
<220>
<221> misc_feature
<222> (16)..(17)
<223> t: 2'-O-MOE-rT
<220>
<221> misc_feature
<222> (18)..(18)
<223> a: 2'-O-MOE-rA
```

20

<222>	misc_feature (19)(19) g: 2'-O-MOE-rG	
	misc_feature (20)(20) a: 2'-O-MOE-rA	
<222>	<pre>misc_feature (2)(3) t: 2'-O-MOE-rT</pre>	
<400> cttctg	19 gcat ccggtttaga	20
<210><211><211><212><213>	18 RNA	
<220> <223>	Synthetic Oligonucleotide Sequence	
<400> ccucuu	20 accu caguuaca	18
<210><211><211><212><213>	18 RNA	
<220> <223>	Synthetic Oligonucleotide Sequence	
<400> gcuauu	21 accu uaacccag 、	18